Intracoronary Ethyl Alcohol or Phenol Injection Ablates Aconitine-Induced Ventricular Tachycardia in Dogs

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The hypothesis whether localized ventricular tachycardia could be ablated by myocardial necrosis induced with chemical agents injected into a coronary artery was tested. In 59 anesthetized dogs, a diagonal branch of the left anterior descending coronary artery was cannulated either occlusively or nonocclusively. Localized ventricular tachycardia was induced by injecting approximately 0.01 ml of 30 μg/ml of aconitine solution into the left ventricular wall perfused by the cannulated diagonal branch in 54 dogs.

In eight untreated control dogs, aconitine-induced ventricular tachycardia lasted 10.2 ± 2.3 minutes or degenerated into ventricular fibrillation after 7.0 ± 4.0 minutes. In the remaining 46 dogs, 1 ml of saline solution, 25, 50 or 100% ethyl alcohol or 0.94 ml (mean [range 0.4 to 2.0]) of 25% phenol at room temperature was injected into the occluded coronary artery and 1 ml of 100% ethyl alcohol at body temperature was injected into the nonoccluded coronary artery. Ventricular tachycardia was eliminated in 9 (82%) of 11 dogs receiving phenol, 7 (88%) of 8 dogs receiving 100% ethyl alcohol occlusively, 6 (75%) of 8 dogs receiving 100% ethyl alcohol nonocclusively and 6 (67%) of 9 dogs receiving 50% ethyl alcohol for an entire follow-up period of 10 to 60 minutes. However, saline solution and 25% ethyl alcohol suppressed ventricular tachycardia only transiently in 8 (53%) of 15 and 3 (60%) of 5 dogs, respectively. Left ventricular end-diastolic pressure rose from 8.0 to 11.2 mm Hg ($p < 0.05$) immediately after injection of 100% ethyl alcohol in seven dogs.

Pathologic examination revealed that transmural myocardial necrosis (involvement greater than the inner one-half of the left ventricular wall) was present in 35 of 41 dogs receiving phenol or alcohol and nontransmural necrosis was present in the remaining 6 dogs. Fibrin or thrombus, or both, was present in the diagonal coronary branch in 6 dogs and adventitial hemorrhage was present in 8 of 41 dogs.

It is concluded that intracoronary injection of 25% phenol or 50 to 100% ethyl alcohol ablates aconitine-induced ventricular tachycardia. Although myocardial necrosis results, this approach may be useful in selected instances, particularly with drugs that may be less necrotizing or more specific for the arrhythmogenic site or that can be injected with greater accuracy into smaller coronary arteries supplying the arrhythmogenic area.

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Ventricular tachyarrhythmias refractory to antiarrhythmic drugs may be treated by surgery, including cryoablation (1). Electrical cardioverters (2) or defibrillators (3) and electrical ablation (4) are also effective in selected patients. Chemical necrosis of the endocardium elevates the ventricular fibrillation threshold (5) and can prevent ischemic related ventricular fibrillation (6), and application of phenol during ventriculotomy can ablate ventricular tachycardia (7). The purpose of this study was to determine whether chemical necrosis produced by intracoronary injection of phenol or ethyl alcohol, thereby avoiding thoracotomy, could ablate aconitine-induced focal ventricular tachycardia.

Methods

Surgical procedures. Fifty-nine mongrel dogs of either sex, weighing 14 to 32 kg, were anesthetized with alpha-chloralose (100 mg/kg body weight). The dogs were intubated with a cuffed endotracheal tube and ventilated with room air using a constant volume-cycled respirator (Harvard model 607). A left thoracotomy was performed in the fifth intercostal space and the heart was suspended in a pericardial cradle. A fluid-filled cannula placed in the femoral artery

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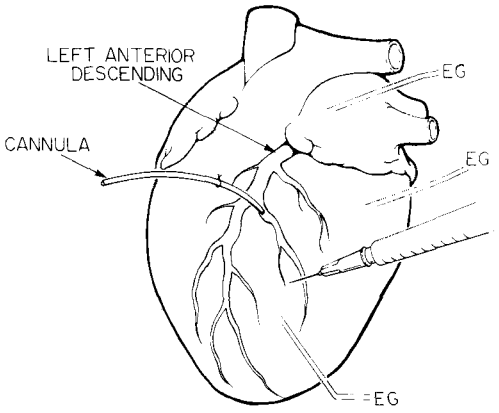


Figure 1. Diagram of the heart showing methods. EG = electrogram.

was connected to a transducer (Statham P23Db) to monitor arterial blood pressure. In seven dogs, a cannula was advanced from the right carotid artery into the left ventricular cavity to record left ventricular pressure. A femoral vein cannula was used to infuse normal saline solution at 100 to 200 ml/h to replace spontaneous fluid losses. The dog was placed on a heating pad, and the thoracotomy was covered by a plastic sheet except during injection of aconitine and test agents. Arterial blood gases and pH were checked and maintained within the physiologic range.

A diagonal branch of the left anterior descending coronary artery was isolated approximately 0.5 cm from its origin and cannulated occlusively with a PE-50 catheter or nonocclusively with a PE-90 catheter (Fig. 1). Occlusive cannulation was chosen initially because of technical considerations. When intracoronary injection of test agents through an occlusively cannulated artery proved effective in suppressing ventricular tachycardia, nonocclusive cannulation was then tested because of the possible clinical relevance. A bipolar plunge electrode was placed in the left atrial wall. Two bipolar plunge electrodes were inserted in the left ventricular wall, one in the area perfused by the cannulated diagonal branch, and the other in a normal area, outside the perfusion zone (Fig. 1).

Study protocol. Aconitine (Sigma), 3 mg, was dissolved in 100 ml of distilled water. Focal ventricular tachycardia was induced with an injection of approximately 0.01 ml of aconitine solution 2 to 3 mm deep into the left ventricular wall through a 26 gauge needle (8). The site of aconitine injection was about 5 mm away from the cannulated diagonal coronary branch, in its obvious area of distribution of flow (Fig. 1). Then 5 to 30 seconds after ventricular tachycardia appeared, the test agents listed in Table 1 were injected through the cannula over 5 to 20 seconds.

Drugs tested. In eight control dogs a diagonal coronary branch was cannulated occlusively as in other groups, but aconitine-induced ventricular tachycardia was untreated. In another five dogs, 1 ml of 100% ethyl alcohol at room temperature was injected into the occluded diagonal branch without aconitine-induced ventricular tachycardia to determine whether ethyl alcohol injection itself induced ventricular tachycardia or ventricular fibrillation spontaneously. In the remaining 46 dogs, the following drugs were tested after sustained ventricular tachycardia was induced with aconitine: 1 ml of normal saline solution at room temperature injected into the occluded diagonal coronary artery in 15 dogs; 0.94 ml (mean [range 0.4 to 2.0 ml]) of 25% phenol dissolved in 100% ethyl alcohol at room temperature injected into the occluded diagonal branch in 12 dogs; in 10 of these dogs saline solution had previously been injected without effect; 1 ml of 100% ethyl alcohol at room temperature injected into the occluded diagonal branch in 9 dogs; in 2 of these dogs, saline had previously been injected without effect; 1 ml of 50% ethyl alcohol at room temperature injected into the occluded diagonal branch in 9 dogs; 1 ml of 25% ethyl alcohol at room temperature injected into the occluded diagonal branch in 5 dogs; 1 ml of 100% ethyl alcohol at body temperature injected into the nonoccluded diagonal branch in 8 dogs.

Surface electrocardiographic (ECG) lead II, an atrial and two ventricular electrograms and arterial blood pressure or

Table 1. Study Groups Among 54 Dogs

Test Agent	Amount	Temperature	Coronary Cannulation	No. of Dogs
None*	None	(−)	Occlusive	8
Saline solution	1 ml	Room	Occlusive	15
25% Phenol	0.9 ml†	Room	Occlusive	12‡
100% Ethyl alcohol	1 ml	Room	Occlusive	9§
100% Ethyl alcohol	1 ml	37 to 38°C	Nonocclusive	8
50% Ethyl alcohol	1 ml	Room	Occlusive	9
25% Ethyl alcohol	1 ml	Room	Occlusive	5

*Sham dogs served as control in which aconitine-induced ventricular tachycardia remained untreated. †Mean value; range 0.4 to 2.0 ml. ‡Ten of 12 dogs received saline injection before phenol injection. §Two of nine dogs received saline injection before ethyl alcohol injection.

left ventricular pressure were recorded at a paper speed of 5, 10, 25 or 50 mm/s (Electronics for Medicine or Gould recorder). In dogs with occlusive coronary cannulation, the follow-up period was 10 to 20 minutes. Dogs with nonocclusive cannulation and dogs in which ethyl alcohol was injected without aconitine injection were monitored for 60 minutes. In the following analysis, transient suppression of ventricular tachycardia was defined as ventricular tachycardia recurring during the follow-up period, and suppression of ventricular tachycardia as ventricular tachycardia not recurring during the entire follow-up period.

Pathologic examination. After the experiment, the heart was removed and fixed in formalin. The heart with occlusive coronary cannulation was removed within 25 minutes after cannulation, and the heart with nonocclusive cannulation was removed within 80 minutes after cannulation. The ventricles were cut in five transverse slices from apex to base. Pathologic assessment was performed (by B.F.W.) without knowledge of the study subgroup. Macroscopically, necrosis was classified as transmural if it involved an area greater than the inner one-half of the left ventricular wall and as nontransmural if it involved a lesser area. All transmural infarcts under this definition become full-thickness infarcts on serial sectioning. Necrosis under each major category was then classified as follows:

Focal-discrete: isolated small nonconfluent zone of necrosis (diameter ≤2 cm).

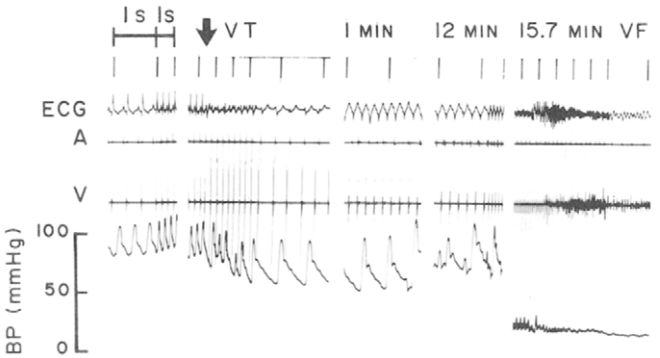
Focal-patchy: more than one focal-discrete nonconfluent zone of necrosis.

Diffuse: confluent zone of necrosis (diameter >2 cm).

Histologic slides were stained with hematoxylin-eosin, Masson's trichrome and Verhoeff's elastic stain to assess myocardial and vessel injury. Myocardial necrosis associated with extravasated erythrocytes that were visible both grossly and microscopically was called hemorrhagic. Arterial damage was assessed for intimal injury, the presence or absence of luminal fibrin or thrombus, or both, and adventitial hemorrhage. When luminal fibrin or thrombus was adherent to the vessel wall, it was presumed to overlie intimal injury. Histologic recognition of the underlying intimal injury was not always established and the cause of the injury (chemical, mechanical or both) was not determined.

Analysis of data. The data are expressed as mean ± SD. The difference among mean values was analyzed using an analysis of variance or an analysis of variance for repeated measurements. When multiple comparisons were made, the *t* test was modified by the Bonferroni method. The difference between two mean values was analyzed using an unpaired *t* test. The incidence of ventricular tachycardia suppression and transmural myocardial infarction was compared using the chi-square test, and multiple comparisons were made using the method of adjusted significance levels of Ryan (9).

Figure 2. Aconitine-induced ventricular tachycardia (VT) in a control dog. Surface electrocardiographic (ECG) lead II, atrial electrogram (A), ventricular electrogram (V) and arterial blood pressure (BP) are arranged from **top** to **bottom.** Each vertical line shows a 1 second interval. **Arrow** indicates the onset of ventricular tachycardia. For 12 minutes after onset of ventricular tachycardia, the cycle length of ventricular tachycardia and blood pressure were fairly stable. Thereafter, blood pressure decreased gradually and ventricular fibrillation (VF) developed 15.7 minutes after the onset of ventricular tachycardia.



Results

Induction of ventricular tachycardia. In all 54 dogs receiving aconitine injection, ventricular tachycardia appeared 159 ± 104 seconds (range 10 to 400) after the injection. In three of eight control dogs, untreated aconitine-induced ventricular tachycardia lasted 10.2 ± 2.3 minutes, and in the remaining five dogs, the tachycardia degenerated into ventricular fibrillation 7.0 ± 4.0 minutes after first appearing. The ventricular tachycardia initiated in the control dog shown in Figure 2 remained stable hemodynamically for 12 minutes. Thereafter blood pressure decreased and ventricular fibrillation developed 15.7 minutes after onset of the tachycardia.

The cycle length of ventricular tachycardia before injection of the test agent is shown in Figure 3. In control dogs, the cycle length of the tachycardia was determined about 30 seconds after its onset. Two dogs whose ventricular tachycardia degenerated into ventricular fibrillation after saline injection but before injection of 25% phenol and 100% ethyl alcohol through an occlusive coronary cannula were excluded from analysis in the 25% phenol group and 100% ethyl alcohol group. Mean cycle length of ventricular tachycardia ranged from 202 to 246 ms and did not differ among the study groups.

Suppression of ventricular tachycardia. A representative example of suppression of ventricular tachycardia with 25% phenol at room temperature administered through an occlusively cannulated coronary artery is shown in Figure 4, and the results of suppression of ventricular tachycardia for all groups are summarized in Figure 5. Saline solution transiently (47 ± 63 seconds) suppressed ventricular tachy-

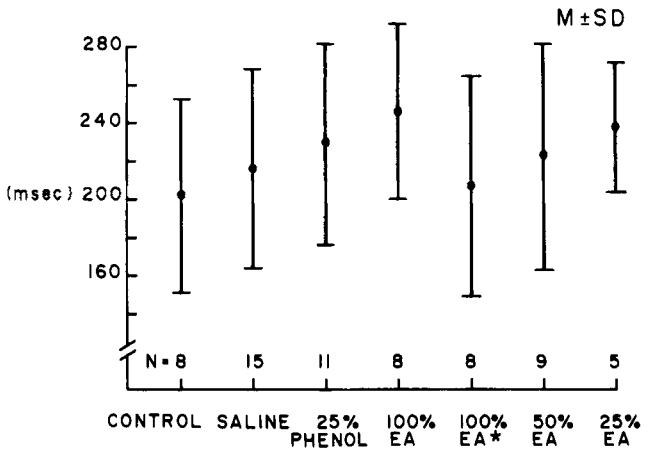


Figure 3. Cycle length of aconitine-induced ventricular tachycardia (VT). EA = ethyl alcohol.*38°C, nonocclusive.

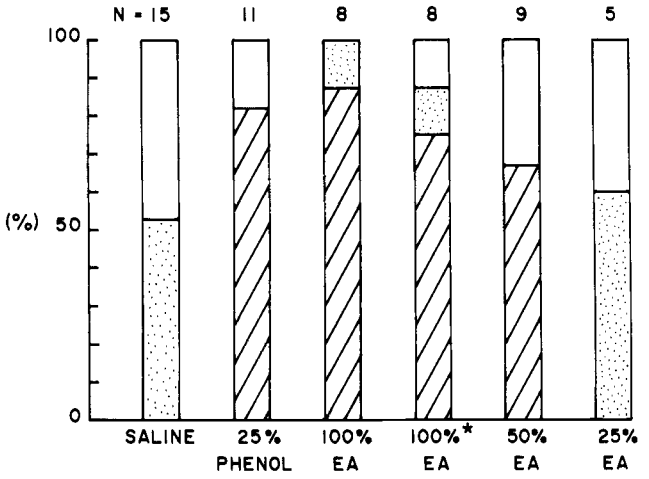
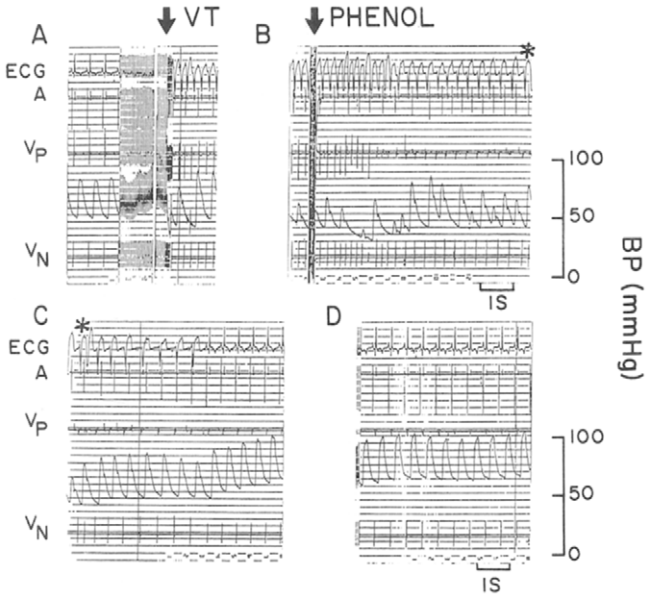


Figure 5. Suppression of ventricular tachycardia (VT) by intracoronary injection of test agents in 46 dogs. Nine dogs received saline and 25% phenol and another dog received saline and 100% ethyl alcohol. **Open bars** indicate ventricular tachycardia that was not affected. **Stippled bars** show transient suppression of ventricular tachycardia, that is, recurrence of ventricular tachycardia during the follow-up period. **Hatched bars** indicate suppression of ventricular tachycardia for the entire follow-up period. EA = ethyl alcohol. *38°C, nonocclusive.

Figure 4. Termination of ventricular tachycardia (VT) with 25% phenol injected through cannulation of an occluded coronary artery. In **each panel,** surface electrocardiographic (ECG) lead II, atrial electrogram (A), ventricular electrogram recorded from the region injected with phenol (V_P), arterial blood pressure (BP) and ventricular electrogram recorded from the normal area (V_N) are arranged from **top** to **bottom. Panel A,** The onset of ventricular tachycardia is shown (**arrow**). **Panel B,** During ventricular tachycardia, 1 ml of 25% phenol at room temperature was injected (**arrow**) over 9 seconds. The cycle length of VT lengthened gradually and sinus rhythm was restored (**panel C**). **Asterisks** in **B** and **C** indicate the identical beat shown at the **top right** and **bottom left.** Note that the ST segment is elevated in the surface ECG and that the ventricular electrogram recorded from the phenol injection site (V_P) decreases in amplitude. **Panel D,** ECG recorded 20 minutes after suppression of ventricular tachycardia demonstrates normal sinus rhythm. ST elevation in the surface ECG is not apparent, but the ventricular electrogram recorded from the phenol injection site (V_P) remains decreased in amplitude.



cardia in eight dogs (53%) and did not affect it in seven. Twenty-five percent phenol and 50 to 100% ethyl alcohol suppressed ventricular tachycardia for the entire follow-up period in 67 to 88% of dogs. The interval between the onset of ventricular tachycardia and the intracoronary injection of test agents, and the time required for the tachycardia to disappear are shown in Table 2. Twenty-five percent ethyl alcohol failed to affect ventricular tachycardia in two (40%) of five dogs and suppressed it only transiently (348 ± 190 seconds) in three (60%) of five dogs. The duration of tran-

Table 2. Time Course of Responses to Test Agent

	Time From Onset of VT to Intracoronary Injection of Test Agent (s)	Time From Injection of Test Agent to VT Disappearance (s)*
Saline solution	13 ± 9	(4 ± 6)
25% Phenol	22 ± 8†	21 ± 21
100% Ethyl alcohol	9 ± 4	28 ± 17 (29)
100% Ethyl alcohol‡	11 ± 6	26 ± 6 (60)
50% Ethyl alcohol	11 ± 6	8 ± 9
25% Ethyl alcohol	16 ± 5	(9 ± 5)

*Data for transient suppression are shown separately in the parentheses. Values for suppression of ventricular tachycardia for the entire follow-up period were not different among four groups of dogs. †Phenol was injected after saline solution failed to suppress ventricular tachycardia (see text). Therefore, this time interval was longer than values for other test agents ($p < 0.01$). However, among agents other than phenol, the time interval was not different. ‡Through a nonocclusive coronary cannulation. VT = ventricular tachycardia.

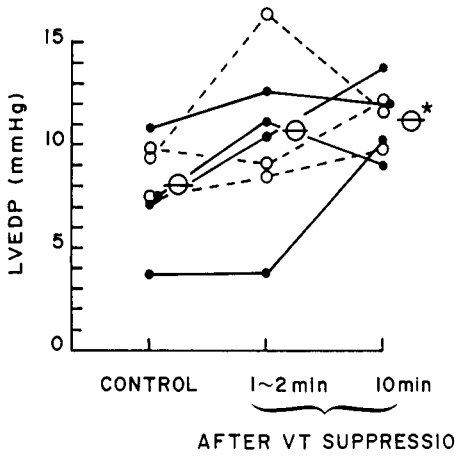


Figure 6. Changes in left ventricular end-diastolic pressure (LVEDP) in seven dogs treated with 100% ethyl alcohol. LVEDP during sinus rhythm was measured before induction of ventricular tachycardia (VT), 1 to 2 minutes after suppression of ventricular tachycardia when left ventricular pressure became stable and 10 minutes after suppression of ventricular tachycardia. **Open circles** show three dogs with occlusive injection and **closed circles** show four dogs with nonocclusive injection of ethyl alcohol, 38°C. *p < 0.05.

sient suppression by 25% ethyl alcohol was significantly longer than that produced by saline solution ($p < 0.001$). The incidence of suppression of ventricular tachycardia for the entire follow-up period was significantly greater in groups treated with 25% phenol and 50 to 100% ethyl alcohol than in groups treated with saline solution and 25% ethyl alcohol ($p < 0.001$). In the whole group, ventricular tachycardia that had not been suppressed by phenol or 50 to 100% ethyl alcohol injection finally degenerated into ventricular fibrillation in 7 of 36 dogs. However, no episodes of ventricular tachycardia or ventricular fibrillation developed in five dogs receiving occlusive injection of 100% ethyl alcohol without aconitine injection during a 60 minute follow-up period after alcohol injection.

Changes in hemodynamics. Changes in left ventricular end-diastolic pressure were analyzed from the pooled data in seven dogs receiving injection of 100% ethyl alcohol (Fig. 6) through occlusive cannulation (three dogs) or nonocclusive cannulation (four dogs). Left ventricular end-diastolic pressure rose significantly in this group from 8.0 to 11.2 mm Hg 10 minutes after suppression of ventricular tachycardia ($p < 0.05$). In four dogs with nonocclusive injection of 100% ethyl alcohol, left ventricular end-diastolic pressure remained elevated at 10.8 mm Hg 60 minutes after suppression of ventricular tachycardia. Systolic and diastolic arterial blood pressure, however, did not differ between control values and values 10 minutes after suppression of ventricular tachycardia in each study group.

ECG changes. Surface ECG lead II showed ST-T changes after suppression of ventricular tachycardia in four of nine dogs treated with phenol, in five of eight dogs treated with occlusive injection of 100% ethyl alcohol, in two of six dogs treated with 50% ethyl alcohol injection and in four of six dogs treated with nonocclusive injection of 100% ethyl alcohol. In four dogs with nonocclusive injection of 100% ethyl alcohol, ST-T changes attenuated progressively, but were still present 60 minutes after termination of ventricular tachycardia.

In six dogs whose ventricular tachycardia was suppressed by nonocclusive alcohol injection, the amplitude of bipolar ventricular electrogram decreased to 19 ± 13% of the control value ($p < 0.001$) at the alcohol-injected sites, but remained at 80 ± 28% of the control value in the noninvolved myocardium (p = NS) 60 minutes after termination of ventricular tachycardia. In other study groups, the amplitude of the bipolar electrogram was also decreased but was not quantitated because of the effects possibly produced by occlusive cannulation alone.

Pathologic examination (Tables 3 and 4). Forty-one hearts treated with phenol or ethyl alcohol were examined. Two hearts in which ventricular fibrillation developed just before an injection of 25% phenol and 100% ethyl alcohol, respectively, into an occluded coronary artery were not included in the pathologic examination. Myocardial necrosis was present on gross and histologic examination in each heart (Fig. 7, Table 2). Of 41 hearts, 35 (85%) had trans-

Table 3. Myocardial Necrosis in 41 Dogs

		Transmural			Nontransmural		
Test Agent	No. of Dogs	Focal-Discrete	Focal-Patchy	Diffuse	Focal-Discrete	Focal-Patchy	Diffuse
25% Phenol	11	4	3	3	1	0	0
100% Ethyl alcohol	8	5	1	1(Hem:1)	1	0	0
100% Ethyl alcohol*	8	2	2(Hem:1)	1	1	1	1
50% Ethyl alcohol	9	6	1	2(Hem:2)	0	0	0
25% Ethyl alcohol	5	3	1	0	0	1	0
Total	41	20	8	7	3	2	1

*Through a nonocclusive cannulation. Hem = hemorrhagic necrosis.

Table 4. Coronary Artery Lesions in 41 Dogs

Test Agent	No. of Dogs	Intimal Injury	Fibrin or Thrombus or Both	Adventitial Hemorrhage
25% Phenol	11	(2)†	2	1
100% Ethyl alcohol	8	(3)	3	1
100% Ethyl alcohol*	8	(1)	1	3
50% Ethyl alcohol	9	0	0	3
25% Ethyl alcohol	5	0	0	0
Total	41	(6)	6	8

*Through a nonocclusive cannulation. †Parentheses indicate that intimal injury was presumed to be present (see text).

mural necrosis (involvement greater than the inner one-half of the left ventricular wall) and 6 (15%) had nontransmural necrosis. Four hearts with transmural myocardial necrosis induced by 50 to 100% ethyl alcohol showed hemorrhagic necrosis. The ratio of transmural versus nontransmural myocardial necrosis did not differ among study groups. In 6 of 41 hearts, luminal fibrin or thrombus, or both, was present in the diagonal coronary branch. In another eight hearts adventitial hemorrhage was present (Table 4).

Phenol or ethyl alcohol failed to suppress ventricular tachycardia in 10 of 28 hearts with focal transmural myocardial necrosis, in 2 of 7 hearts with diffuse transmural necrosis and in 1 of 6 hearts with focal nontransmural necrosis.

Discussion

Major findings. In the present study, intracoronary injection of 25% phenol and 50 to 100% ethyl alcohol suppressed aconitine-induced ventricular tachycardia in 67 to 88% of dogs. Twenty-five percent ethyl alcohol was not effective. Left ventricular end-diastolic pressure rose slightly but significantly after injection of 100% ethyl alcohol. Pathologic examination revealed that myocardial necrosis

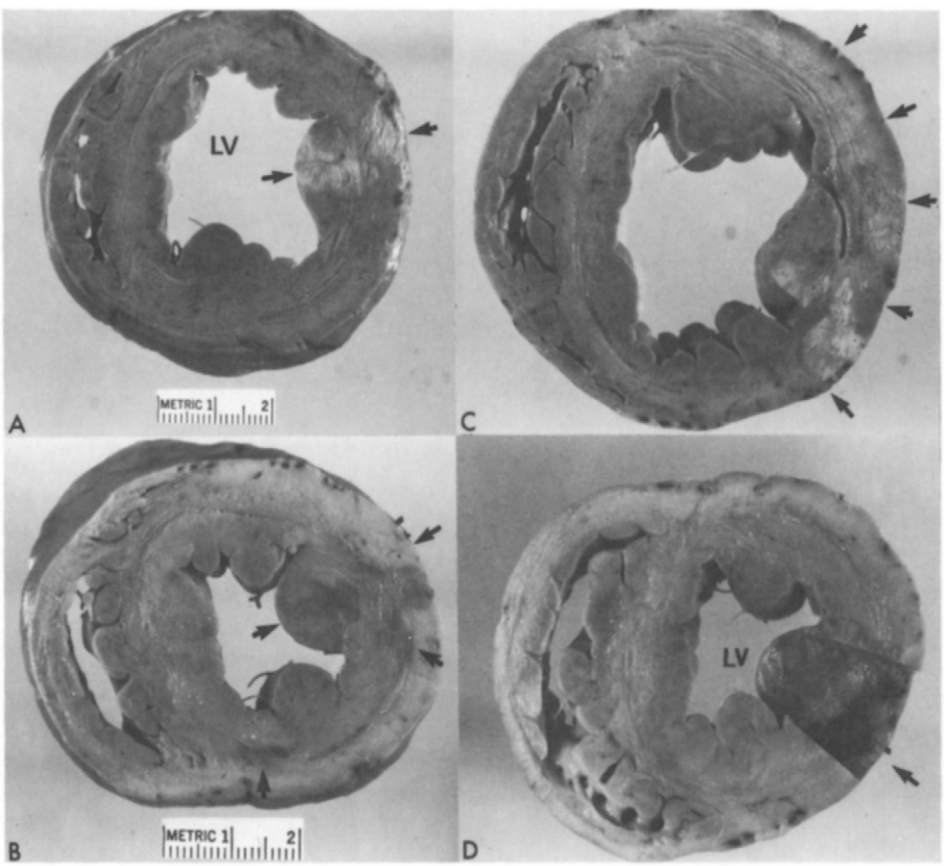


Figure 7. Composite of transverse ventricular slices showing classification of transmural infarction. **A,** Focal-discrete necrosis, which is focal and localized to the anterolateral papillary muscle and adjacent free wall (**arrows**). **B,** Focal-patchy necrosis, which involves two discrete and focal zones (**arrows**). **C,** Diffuse necrosis, which involves extensive contiguous areas of the anterolateral left ventricle (LV). Diffuse necrosis also extended from the ventricular apex to base. In contrast, focal necrosis was confined to the basal, middle or apical third of the left ventricle. **D,** Hemorrhagic necrosis, which is transmural and associated with grossly visible extravasated erythrocytes (**arrow**). The sharp border zone is due to a cut to remove the tissue block for histologic examination.

was present in each heart. In 85% of the hearts, necrosis involved an area greater than the inner one-half of the left ventricular wall. In 34% of the hearts, luminal fibrin or thrombus, or both, or adventitial hemorrhage was present.

Mechanisms for suppression of ventricular tachycardia. Cooling of the focus of aconitine-induced ventricular tachycardia probably explains the transient suppression of ventricular tachycardia by saline injection at room temperature, as noted previously (10). Intracoronary injection of phenol or 50 to 100% ethyl alcohol produced tissue necrosis, presumably with resultant loss of electrical activity at the aconitine injection site, although the correlation between this site and myocardial necrosis was not determined in the present study. We conjecture that ventricular tachycardia was suppressed by tissue necrosis involving the focus of ventricular tachycardia itself or surrounding tissue, or both, that prevented propagation of activation from the focus (exit block).

Pathologic changes. In each heart receiving 25% phenol and 50 to 100% ethyl alcohol, myocardial necrosis was present. The heart was removed within 25 minutes after occlusive coronary artery cannulation. This period of time is too short for myocardial necrosis to be detected by histologic examination without special staining. Myocardial necrosis was also produced in the hearts with nonocclusive coronary artery cannulation. Therefore, myocardial necrosis observed histologically in the heart with occlusive cannulation appears to be attributable to phenol or ethyl alcohol. Although the ratio of focal versus diffuse transmural necrosis did not differ among study groups, the severity of myocardial damage tended to be greater in the phenol and 50 to 100% ethyl alcohol groups than in the 25% ethyl alcohol group. First, diffuse transmural myocardial necrosis was not present in the 25% ethyl alcohol group, whereas it occurred in one to three dogs in each of the other groups. Second, hemorrhagic necrosis, a marker for severe myocardial damage (11), was present in the 50 to 100% ethyl alcohol groups but was not found in the 25% ethyl alcohol group. These findings are consistent with a previous study (12) showing that a lower concentration of ethyl alcohol fails to induce tissue damage, and may explain the ineffectiveness of 25% ethyl alcohol in suppressing ventricular tachycardia in the present study. The amount of myocardial necrosis in the present study may be larger than that induced by electrical ablation techniques (13,14). In seven hearts, luminal fibrin or thrombus or both was present in the diagonal coronary branch. This might be attributed, at least in part, to thrombosis-inducing properties of ethyl alcohol (15) without concomitant intimal injury. Twenty-five percent ethyl alcohol did not induce arterial damage but did not suppress ventricular tachycardia.

Methodologic considerations. Aconitine elicits early afterdepolarizations with resultant repetitive firing (16). When injected into the atrial or ventricular wall, aconitine induces atrial or ventricular tachycardia, flutter or fibrillation (8,10). Because we wished to induce ventricular tachycardia from a focus known to be in the distribution of the cannulated diagonal coronary artery, aconitine served as an ideal agent even though the electrophysiologic mechanism of the ventricular tachycardia probably differed from that of most clinical ventricular tachycardias.

Clinically, ethyl alcohol is injected into arteries to treat malignant tumors of the kidney, liver and other organs because of its protein-denaturing and vascular thrombosis-forming properties (17,18). Potential complications of ethyl alcohol injection include temporary or irreversible organ failure, and pulmonary or systemic embolization of nontarget tissues with high concentrations of ethyl alcohol (19). In a recent study (20), ventricular fibrillation developed immediately after selective renal artery embolization with absolute ethyl alcohol at doses of >0.18 ml/kg in 3 of 11 dogs. In 7 of 36 dogs in the present study, ventricular tachycardia that had not been suppressed by phenol or 50 to 100% ethyl alcohol injection finally degenerated into ventricular fibrillation. In five dogs receiving 100% ethyl alcohol without aconitine injection, ventricular fibrillation did not appear for the entire follow-up period of 60 minutes and in five of eight control dogs aconitine-induced ventricular tachycardia degenerated into ventricular fibrillation. Therefore, it is likely that ventricular fibrillation that appeared in the seven treated dogs of the present study was a sequela of aconitine-induced ventricular tachycardia.

Although the blood level of ethyl alcohol was not determined in this study, a canine experimental study (20) showed that the maximal ethyl alcohol level in the aortic blood was 0.142 ± 0.159 vol% (range 0.001 to 0.399) after injection of 2.14 ± 0.44 ml (range 0.99 to 4.2) of 100% ethyl alcohol into the renal artery. Because 1 ml of 100% ethyl alcohol was the maximal dose used in the present study, it is unlikely that arterial alcohol concentrations exceeded a mean value of about 0.1 to 0.15 vol%.

Limitations and future applications. Our study is limited for several reasons. First, aconitine-induced ventricular tachycardia probably differs from ventricular tachycardia observed in patients, although triggered activity, possibly due to early afterdepolarizations, has been considered as a potential mechanism for ventricular tachycardia in some patients (21). Second, precise correlation between the aconitine injection site and myocardial necrosis was not determined. Third, if a suitable coronary artery in the distribution of the origin of the ventricular tachycardia cannot be cannulated or is occluded, as may be the case in some patients with coronary artery disease, the present technique may not be applicable. However, it is possible that interruption of only a part of the reentrant pathway or exit to the ventricular myocardium, such as might occur in patients with ventric-

ular tachycardia related to coronary artery disease, may be equally effective. Fourth, the amount of tissue damage produced by phenol or ethyl alcohol injection into a diagonal coronary branch is considerable. In the future, cannulation of smaller arteries, possibly using angioplasty catheters, may spare more myocardium, although it may be difficult to position the catheter in a small, patent artery that perfuses myocardium relevant to the tachycardia.

Using more specific chemicals may be appropriate. For example, drugs preferentially concentrated in damaged areas made unique by virtue of depolarized cells, elevated intracellular calcium concentrations or other specific qualities of arrhythmogenic cells may be possible in the future. We have injected phenol retrogradely into the coronary sinus, but considerable necrosis of the subendocardium results. That approach may be better for treating ventricular tachycardia of subendocardial origin in patients with coronary artery disease. Finally, long-term follow-up data are necessary to determine hemodynamic and electrophysiologic consequences of this technique. Although the present approach using alcohol or phenol may not be the answer for treating ventricular tachycardia, this study establishes a concept, that of chemical ablative therapy by coronary perfusion of an anatomic substrate for ventricular arrhythmias. Broadened and refined, this approach might be applicable for treating other tachycardias as well.

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